Harris, A.
09/810385

FILE 'HCAPLUS, MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, JAPIO' ENTERED AT 11:33:43 ON 31 OCT 2003

L1 121 SEA ABB=ON PLU=ON LAUGHON A?/AU

L2 24 SEA ABB=ON PLU=ON L1 AND (SMAD OR EVI1 OR EVII OR (EVI OR SIP)(W)(1 OR I) OR TGIF OR SIP1 OR SIPI OR SCHNURRI OR DROSOPHIL?(S)(MAD OR MEDEA) OR TG(W) INTERACT?(W) FACTOR)

L3 6 DUP REM L2 (18 DUPLICATES REMOVED)

L3 ANSWER 1 OF 6 HCAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 1

ACCESSION NUMBER: 2002:736875 HCAPLUS
DOCUMENT NUMBER: 137:242137
TITLE: Compositions and methods for negative regulation of TGF-β pathways
INVENTOR(S): **Laughon, Allen S.**
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 15 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002137662	A1	20020926	US 2001-810385	20010316
WO 2002076466	A1	20021003	WO 2002-US8133	20020315

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-810385 A 20010316

AB Methods for screening for compds. that are neg. regulators of TGF-β-regulated gene expression in mammalian cells are provided, including compns. identified therefrom.

L3 ANSWER 2 OF 6 HCAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 2

ACCESSION NUMBER: 2001:411533 HCAPLUS
DOCUMENT NUMBER: 136:97165
TITLE: Repression of Dpp targets by binding of brinker to Mad sites
AUTHOR(S): Kirkpatrick, Heidi; Johnson, Kirby; **Laughon, Allen**
CORPORATE SOURCE: Laboratory of Genetics, University of Wisconsin, Madison, WI, 53706, USA
SOURCE: Journal of Biological Chemistry (2001), 276(21), 18216-18222
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal

LANGUAGE: English

AB Signaling by decapentaplegic (Dpp), a Drosophila member of the transforming growth factor (TGF) β superfamily of growth factors, has recently been shown to activate targets such as vestigial (vg) indirectly through neg. regulation of brinker (brk). Here we show that the Brk protein functions as a repressor by binding to Dpp response elements. The Brk DNA binding activity was localized to an amino-terminal region containing a putative homeodomain. Brk bound to a Dpp response element of the Ultrabithorax (Ubx) midgut enhancer at a sequence that overlaps a binding site for the **Smad** protein, Mothers Against Dpp (Mad). Furthermore, Brk was able to compete with Mad for occupancy of this binding site. This recognition of overlapping binding sites provides a potential explanation for why the G/C-rich Mad binding site consensus differs the Smad3/Smad4 binding site consensus. We also found that the Dpp response element from Ubx was more sensitive than the vg quadrant enhancer to repression by Brk. This difference correlates with short-range activation of Ubx by Dpp in the visceral mesoderm, whereas vg exhibits a long-range response to Dpp in the wing imaginal disk, indicating that Brk binding sites may play a critical role in limiting thresholds for activation by Dpp. Finally, we provide evidence that Brk is capable of functioning as an active repressor. Thus, whereas Brk and Mad compete for regulation of Ubx and vg, Brk may regulate other Dpp targets without direct involvement of Mad.

REFERENCE COUNT: 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 3 OF 6 HCAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 3

ACCESSION NUMBER: 2000:219108 HCAPLUS
DOCUMENT NUMBER: 132:260665
TITLE: Compositions and methods for identifying and testing TGF-β pathway agonists and antagonists
INVENTOR(S): **Laughon, Allen**; Johnson, Kirby; Kim, Jaeseob
PATENT ASSIGNEE(S): Ophidian Pharmaceuticals, Inc., USA
SOURCE: U.S., 50 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6046165	A	20000404	US 1997-880729	19970623

PRIORITY APPLN. INFO.: US 1997-880729 19970623

AB The invention provides compns. and methods of identifying and testing TGF-β pathway agonists and antagonists, and in particular compns. comprising Mothers against DPP (MAD) proteins and related **Smad** polypeptides which exhibit sequence-specific DNA-binding activity. The invention also provides novel DNA sequences (SEQ ID NO:19); (SEQ ID NO:20); (SEQ ID NO:21) that are bound with high affinity by **Drosophila MAD** protein. This protein is useful for identifying compds. that will enhance or interfere with MAD protein-DNA binding.

REFERENCE COUNT: 103 THERE ARE 103 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 4 OF 6 HCAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 4
ACCESSION NUMBER: 1999:467078 HCAPLUS
DOCUMENT NUMBER: 131:224368
TITLE: Interaction of **Smad** complexes with tripartite DNA-binding sites
AUTHOR(S): Johnson, Kirby; Kirkpatrick, Heidi; Comer, Allen; Hoffmann, F. Michael; **Laughon, Allen**
CORPORATE SOURCE: Laboratory of Genetics, University of Wisconsin-Madison, Madison, WI, 53706, USA
SOURCE: Journal of Biological Chemistry (1999), 274(29), 20709-20716
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The **Smad** family of transcription factors function as effectors of transforming growth factor-β signaling pathways. **Smads** form heteromultimers capable of contacting DNA through the amino-terminal MH1 domain. The MH1 domains of Smad3 and Smad4 have been shown to bind to the sequence 5'-GTCT-3'. Here the authors show that Smad3 and Smad4 complexes can contact three abutting GTCT sequences and that arrays of such sites elevate reporter expression relative to arrays of binding sites containing only two GTCTs. Smad3/4 complexes bound synergistically to probes containing two of the four possible arrangements of three GTCT sequences and showed a correlated ability to synergistically activate transcription through these sites. Purified Smad3 and Smad4 were both able to contact three abutting GTCT sequences and reporter expts. indicated that either protein could mediate contact with all three GTCTs. In contrast, the Smad4 MH1 domain was essential for reporter activation in combination with Smad1. Together, these results show that **Smad** complexes are flexible in their ability to interact with abutting GTCT triplets. In contrast, **Smads** have high affinity for only one orientation of abutting GTCT pairs. Functional **Smad**-binding sites within several native response elements contain degenerate GTCT triplets, suggesting that trimeric **Smad**-DNA interaction may be relevant in vivo.
REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 5 OF 6 HCAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 5
ACCESSION NUMBER: 1997:470466 HCAPLUS
DOCUMENT NUMBER: 127:159293
TITLE: **Drosophila Mad** binds to DNA and directly mediates activation of vestigial by decapentaplegic
AUTHOR(S): Kim, Jaeseob; Johnson, Kirby; Chen, Hui Ju; Carroll, Sean; **Laughon, Allen**
CORPORATE SOURCE: Howard Hughes Med. Inst. and Lab. Mol. Biol., Univ. Wisconsin, Madison, WI, 53706, USA

SOURCE: Nature (London) (1997), 388(6639), 304-308
CODEN: NATUAS; ISSN: 0028-0836
PUBLISHER: Macmillan Magazines
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The N-terminal domain of the **Drosophila** Mothers against dpp protein (**Mad**), a mediator of Dpp signaling, possesses a sequence-specific DNA-binding activity that becomes apparent when C-terminal residues are removed. Mad binds to and is required for the activation of an enhancer within the vestigial wing-patterning gene in cells across the entire developing wing blade. Mad also binds to Dpp-response elements in other genes. These results suggest that Dpp signaling regulates gene expression by activating Mad binding to target gene enhancers.

L3 ANSWER 6 OF 6 HCAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 6

ACCESSION NUMBER: 1995:909240 HCAPLUS
DOCUMENT NUMBER: 124:25918
TITLE: A Drosophila protein related to the human zinc finger transcription factor PRDII/MBPI/HIV-EP1 is required for dpp signaling
AUTHOR(S): Staehling-Hampton, Karen; **Laughon, Allen S.**; Hoffmann, F. Michael
CORPORATE SOURCE: Lab. Genet., Univ. Wisconsin Med. Sch., Madison, WI, 43706, USA
SOURCE: Development (Cambridge, United Kingdom) (1995), 121(10), 3393-403
CODEN: DEVPED; ISSN: 0950-1991
PUBLISHER: Company of Biologists
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Little is known about the signal transduction pathways by which cells respond to mammalian TGF-βs or to decapentaplegic (dpp), a Drosophila TGF-β-related factor. The genetic and mol. characterization of Drosophila **schnurri** (shn), a putative transcription factor implicated in dpp signaling, is described. The shn protein has 8 zinc fingers and is related to a human transcription factor, PRDII/MBPI/HIV-EP1, that binds to nuclear factor-κB-binding sites and activates transcription from the HIV long terminal repeat (LTR). Shn mRNA is expressed in a dynamic pattern in the embryo that includes most of the known target tissues of dpp, including the dorsal blastoderm, the mesodermal germ layer, and parasegments 4 and 7 of the midgut. Mutations in shn affect several developmental processes regulated by dpp, including induction of visceral mesoderm cell fate, dorsal/ventral patterning of the lateral ectoderm, and wing vein formation. Absence of shn function blocks the expanded expression of the homeodomain protein bagpipe in the embryonic mesoderm caused by ectopic dpp expression, illustrating a requirement for shn function downstream of dpp action. Thus, shn function is critical for cells to respond properly to dpp and propose that shn protein is the first identified downstream component of the signal transduction pathway used by dpp and its receptors.

FILE 'REGISTRY' ENTERED AT 11:39:22 ON 31 OCT 2003
E "TRANSFORMING GROWTH FACTOR-B"/CN
L4 5 S "TRANSFORMING GROWTH FACTOR-B"?/CN
L5 41 S "TRANSFORMING GROWTH FACTOR-B"?/CN

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L6          46 S L4 OR L5
L7         184 S BONE MORPHOGENETIC PROTEIN ?/CN
L8         132 S ACTIVIN ?/CN
L9         361 S L6 OR L7 OR L8

     FILE 'HCAPLUS' ENTERED AT 11:41:43 ON 31 OCT 2003
L4           5 SEA FILE=REGISTRY ABB=ON  PLU=ON  "TRANSFORMING GROWTH
               FACTOR-B"?/CN
L5          41 SEA FILE=REGISTRY ABB=ON  PLU=ON  "TRANSFORMING GROWTH
               FACTOR-B"?/CN
L6          46 SEA FILE=REGISTRY ABB=ON  PLU=ON  L4 OR L5
L7         184 SEA FILE=REGISTRY ABB=ON  PLU=ON  BONE MORPHOGENETIC
               PROTEIN ?/CN
L8         132 SEA FILE=REGISTRY ABB=ON  PLU=ON  ACTIVIN ?/CN
L9         361 SEA FILE=REGISTRY ABB=ON  PLU=ON  L6 OR L7 OR L8
L10      31551 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L9 OR (TRANSFORM?
               GROWTH FACTOR OR TGF)(W)(B OR BETA) OR ACTIVIN OR BONE
               MORPHOGENET? PROTEIN OR BMP OR TGFB
L11       1640 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L10 AND (SMAD OR EVI1
               OR EVII OR (EVI OR SIP)(W)(1 OR I) OR TGIF OR SIP1 OR
               SIPI OR SCHNURRI OR DROSOPHIL?(S)(MAD OR MEDEA MOTHER?(2W
               )DPP) OR TG(W)INTERACT?(W)FACTOR OR SHN)
L12          12 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L11 AND (CTBP# OR
               DCTBP# OR C(W)TERMIN?(W)BIND?)

L12  ANSWER 1 OF 12  HCAPLUS  COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER:         2003:409169  HCAPLUS
DOCUMENT NUMBER:          138:380506
TITLE:                    Genes that are differentially expressed during
                          erythropoiesis and their diagnostic and
                          therapeutic uses
INVENTOR(S):              Brissette, William H.; Neote, Kuldeep S.;
                          Zagouras, Panayiotis; Zenke, Martin; Lemke,
                          Britt; Hacker, Christine
PATENT ASSIGNEE(S):       Pfizer Products Inc., USA; Max-Delbruck-Centre
                          for Molecular Medicine
SOURCE:                   PCT Int. Appl., 285 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   2
PATENT INFORMATION:

     PATENT NO.        KIND  DATE          APPLICATION NO.  DATE
     ---------------   ----  --------      ---------------  --------
     WO 2003038130      A2   20030508      WO 2002-XA34888  20021031
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ,
             LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ,
             NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ,
             TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM,
             AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE,
             BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU,
             MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ,
             GW, ML, MR, NE, SN, TD, TG
     WO 2003038130      A2   20030508      WO 2002-US34888  20021031
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W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-335048P P 20011031
US 2001-335183P P 20011102
WO 2002-US34888 A 20021031

AB The present invention provides mol. targets that regulate erythropoiesis. Groups of genes or their encoded gene products comprise panels of the invention and may be used in therapeutic intervention, therapeutic agent screening, and in diagnostic methods for diseases and/or disorders of erythropoiesis. The panels were discovered using gene expression profiling of erythroid progenitors with Affymetrix HU6800 and HG-U95Av2 chips. Cells from an in vitro growth and differentiation system of SCF-Epo dependent human erythroid progenitors, E-cadherin+/CD36+ progenitors, cord blood, or CD34+ peripheral blood stem cells were analyzed. The HU6800 chip contains probes from 13,000 genes with a potential role in cell growth, proliferation, and differentiation and the HG-U95Av2 chip contains 12,000 full-length, functionally-characterized genes. [This abstract record is one of two records for this document necessitated by the large number of index entries required to fully index the document and publication system constraints.].

IT **479908-67-3 480121-54-8**
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(amino acid sequence; genes that are differentially expressed during erythropoiesis and their diagnostic and therapeutic uses)

L12 ANSWER 2 OF 12 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2003:389319 HCAPLUS
DOCUMENT NUMBER: 139:144804
TITLE: Regulation of **Smad** signaling through a differential recruitment of coactivators and corepressors by ZEB proteins
AUTHOR(S): Postigo, Antonio A.; Depp, Jennifer L.; Taylor, Jennifer J.; Kroll, Kristen L.
CORPORATE SOURCE: Division of Molecular Oncology, Department of Internal Medicine, Washington Univ. Sch. Med., St. Louis, MO, 63110, USA
SOURCE: EMBO Journal (2003), 22(10), 2453-2462
CODEN: EMJODG; ISSN: 0261-4189
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Balancing signals derived from the **TGFβ** family is crucial for regulating cell proliferation and differentiation, and in establishing the embryonic axis during development. **TGFβ /BMP** signaling leads to the activation and nuclear translocation of **Smad** proteins, which activate transcription of specific target genes by

recruiting P/CAF and p300. The two members of the ZEB family of zinc finger factors (ZEB-1/δEF1 and ZEB-2/ **SIP1**) regulate **TGFβ** /**BMP** signaling in opposite ways: ZEB-1/δEF1 synergizes with **Smad** -mediated transcriptional activation, while ZEB-2/**SIP1** represses it. Here the authors report that these antagonistic effects by the ZEB proteins arise from the differential recruitment of transcriptional coactivators (p300 and P/CAF) and corepressors (**CtBP**) to the **Smads**. Thus, while ZEB-1/δEF1 binds to p300 and promotes the formation of a p300-**Smad** transcriptional complex, ZEB-2/**SIP1** acts as a repressor by recruiting **CtBP**. This model of regulation by ZEB proteins also functions in vivo, where they have opposing effects on the regulation of **TGFβ** family-dependent genes during Xenopus development.

IT **114949-22-3, Activin**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(signal transduction by; regulation of **Smad** signaling through a differential recruitment of coactivators and corepressors by ZEB proteins)

REFERENCE COUNT: 72 THERE ARE 72 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 3 OF 12 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:937303 HCAPLUS
DOCUMENT NUMBER: 138:20443
TITLE: Endocrine disruptor screening using DNA chips of endocrine disruptor-responsive genes
INVENTOR(S): Kondo, Akihiro; Takeda, Takeshi; Mizutani, Shigetoshi; Tsujimoto, Yoshimasa; Takashima, Ryokichi; Enoki, Yuki; Kato, Ikunoshin
PATENT ASSIGNEE(S): Takara Bio Inc., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 386 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2002355079	A2	20021210	JP 2002-69354	20020313

PRIORITY APPLN. INFO.:
JP 2001-73183 A 20010314
JP 2001-74993 A 20010315
JP 2001-102519 A 20010330

AB A method and kit for detecting endocrine-disrupting chems. using DNA microarrays are claimed. The method comprises preparing a nucleic acid sample containing mRNAs or cDNAs originating in cells, tissues, or organisms which have been brought into contact with a sample containing the endocrine disruptor. The nucleic acid sample is hybridized with DNA microarrays having genes affected by the endocrine disruptor or DNA fragments originating in these genes have been fixed. The results obtained are then compared with the results obtained with the control sample to select the gene affected by the endocrine disruptor. Genes whose expression is altered by tri-Bu tin, 4-octaphenol, 4-nonylphenol, di-N-Bu phthalate, dichlorohexyl phthalate, octachlorostyrene, benzophenone, diethylhexyl phthalate,

diethylstilbestrol (DES), and 17-β estradiol (E2), were found in mice by DNA chip anal.

L12 ANSWER 4 OF 12 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:736875 HCAPLUS
DOCUMENT NUMBER: 137:242137
TITLE: Compositions and methods for negative regulation of **TGF**-β pathways
INVENTOR(S): Laughon, Allen S.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 15 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002137662	A1	20020926	US 2001-810385	20010316
WO 2002076466	A1	20021003	WO 2002-US8133	20020315

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-810385 A 20010316
AB Methods for screening for compds. that are neg. regulators of **TGF**-β -regulated gene expression in mammalian cells are provided, including compns. identified therefrom.
IT **114949-22-3, Activin**
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(compns. and screening methods for neg. regulation of **TGF** -β pathways)

L12 ANSWER 5 OF 12 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:521969 HCAPLUS
DOCUMENT NUMBER: 137:90000
TITLE: Protein-protein interactions in adipocyte cells and method for selecting modulators of these interactions
INVENTOR(S): Legrain, Pierre; Marullo, Stefano; Jockers, Ralf
PATENT ASSIGNEE(S): Hybrigenics, Fr.; Centre National De La Recherche Scientifique
SOURCE: PCT Int. Appl., 125 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002053726	A2	20020711	WO 2001-EP15423	20011228
WO 2002053726	A3	20030313		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2003040089	A1	20030227	US 2002-38010	20020102

PRIORITY APPLN. INFO.: US 2001-259377P P 20010102

AB The present invention relates to protein-protein interactions of adipocyte. More specifically, the present invention relates to complexes of polypeptides, or polynucleotides encoding the polypeptides, fragments of the polypeptides, antibodies to the complexes. Selected Interacting Domains (SID) which are identified due to the protein-protein interactions, methods for screening drugs for agents which modulate the interaction of proteins, and pharmaceutical compns. that are capable of modulating the protein-protein interactions are further disclosed.

L12 ANSWER 6 OF 12 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2002:340502 HCAPLUS

DOCUMENT NUMBER: 137:61224

TITLE: The t(3;21) fusion product, AML1/**Evi-1** blocks AML1-induced transactivation by recruiting **CtBP**

AUTHOR(S): Izutsu, Koji; Kurokawa, Mineo; Imai, Yoichi; Ichikawa, Motoshi; Asai, Takashi; Maki, Kazuhiro; Mitani, Kinuko; Hirai, Hisamaru

CORPORATE SOURCE: Department of Hematology and Oncology, Graduate School of Medicine, University of Tokyo, Tokyo, 113-8655, Japan

SOURCE: Oncogene (2002), 21(17), 2695-2703
CODEN: ONCNES; ISSN: 0950-9232

PUBLISHER: Nature Publishing Group

DOCUMENT TYPE: Journal

LANGUAGE: English

AB AML1/**Evi-1** is a chimeric protein that is derived from t(3;21), found in blastic transformation of chronic myelogenous leukemia. It is composed of the N-terminal AML1 portion with the DNA-binding Runt domain and the C-terminal **Evi-1** portion. It has been shown to dominantly repress AML1-induced transactivation. The mechanism for it has been mainly attributed to competition with AML1 for the DNA-binding and for the interaction with PEBP2β (CBFβ), a partner protein which heterodimerizes with AML1. It was recently found that **Evi-1** interacts with **C-terminal binding** protein (**CtBP**) to repress **TGF-beta**.-induced transactivation. Here, we demonstrate that AML1/**Evi-1** interacts with **CtBP** in SKH1 cells, a leukemic cell line which endogenously overexpresses AML1/

Evi-1 and that AML1/**Evi-1** requires the interaction with **CtBP** to repress AML1-induced transactivation. The association with **CtBP** is also required when AML1/**Evi-1** blocks myeloid differentiation of 32Dcl3 cells induced by granulocyte colony-stimulating factor. Taken together, it is suggested that one of the mechanisms for AML1/**Evi-1**-associated leukemogenesis should be an aberrant recruitment of a corepressor complex by the chimeric protein.

REFERENCE COUNT: 58 THERE ARE 58 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 7 OF 12 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:185378 HCAPLUS
DOCUMENT NUMBER: 136:212896
TITLE: Gene markers useful for detecting skin damage in response to ultraviolet radiation
INVENTOR(S): Blumenberg, Miroslav
PATENT ASSIGNEE(S): New York University School of Medicine, USA
SOURCE: PCT Int. Appl., 274 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002020849	A2	20020314	WO 2001-US28214	20010907
WO 2002020849	A3	20030703		
W: AU, CA, JP, SG				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
AU 2001090699	A5	20020322	AU 2001-90699	20010907

PRIORITY APPLN. INFO.: US 2000-231061P P 20000908
WO 2001-US28214 W 20010907

AB The cellular response to UV radiation exposure has been characterized on the mol. level through the use of high d. gene array technol. Nucleic acid mols. and protein mols., the expression of which are repressed or induced in response to UV radiation exposure, are identified according to a temporal pattern of altered expression post UV radiation exposure. Methods are disclosed that utilized these UV radiation-regulated mols. as markers for UV radiation exposure. Other screening methods of the invention are designed for the identification of compds. that modulate the response of a cell to UV radiation exposure. The invention also provides compns. useful for drug screening or pharmaceuticals purposes.

IT **114949-22-3, Activin**
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(βB; gene markers useful for detecting skin damage in response to UV radiation)

L12 ANSWER 8 OF 12 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:185375 HCAPLUS
DOCUMENT NUMBER: 136:212895
TITLE: Screening methods to identify compounds that

modulate a gene expression response of a cell to ultraviolet radiation exposure
INVENTOR(S): Blumenberg, Miroslav
PATENT ASSIGNEE(S): New York University, USA
SOURCE: PCT Int. Appl., 459 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002020846	A2	20020314	WO 2001-US28040	20010907
WO 2002020846	A3	20030925		
W: AU, CA, JP, SG				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
US 2002090624	A1	20020711	US 2001-947870	20010906
AU 2001090658	A5	20020322	AU 2001-90658	20010907

PRIORITY APPLN. INFO.: US 2000-231454P P 20000908
WO 2001-US28040 W 20010907

AB The cellular response to UV radiation exposure has been characterized on the mol. level through the use of high d. gene array technol. Nucleic acid mols. and protein mols., the expression of which are repressed or induced in response to UV radiation exposure, are identified according to a temporal pattern of altered expression post UV radiation exposure. Gene and protein sequences regulated by exposure to UV-B or UV-A radiation in cultures of epidermal keratinocytes from human foreskin are provided. Methods are disclosed that utilized these UV radiation-regulated mols. as markers for UV radiation exposure. Other screening methods of the invention are designed for the identofication of compds. that modulate the response of a cell to UV radiation exposure. The invention also provides compns. useful for drug screening or pharmaceutical purposes.

IT **114949-22-3, Activin**
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(βB; screening methods to identify compds. that modulate a gene expression response of a cell to UV radiation exposure)

L12 ANSWER 9 OF 12 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:825133 HCAPLUS
DOCUMENT NUMBER: 136:322953
TITLE: Oncogenic mechanisms of **Evi-1** protein
AUTHOR(S): Hirai, Hisamaru; Izutsu, Koji; Kurokawa, Mineo; Mitani, Kinuko
CORPORATE SOURCE: Department of Hematology and Oncology, Graduate School of Medicine, University of Tokyo, Tokyo, 113-8655, Japan
SOURCE: Cancer Chemotherapy and Pharmacology (2001), 48(Suppl. 1), S35-S40
CODEN: CCPHDZ; ISSN: 0344-5704
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Although **Evi-1** is thought to promote growth or block differentiation in some cell types, its biol. functions have not been elucidated. To explore the mechanisms underlying **Evi-1**-induced oncogenesis, we investigated whether **Evi-1** affects the signaling of **transforming growth factor .beta** . (**TGF-β**), which inhibits proliferation of a wide range of cell types and is one of the most studied growth regulatory factors. We demonstrated that **Evi-1** represses **TGF-β** signaling and antagonizes its growth-inhibitory effects. Two sep. regions of **Evi-1** are responsible for this repression, one of which is the first zinc-finger domain. Through this domain, **Evi-1** phys. interacts with Smad3, an intracellular mediator of **TGF-β** signaling, thereby suppressing the transcriptional activity of Smad3. These results define a novel function of **Evi-1** as a repressor of signaling components of **TGF-β** . We also demonstrated that **Evi-1** represses **Smad**-induced transcriptional activation by recruiting **CtBP** as a corepressor. **Evi-1** assocs. with **CtBP1** through one of the **CtBP**-binding consensus motifs within the region from amino acid 544 to 607, and this association is required for the efficient inhibition of **TGF-β** signaling. A specific histone deacetylase (HDAc) inhibitor, trichostatin A (TSA), alleviates **Evi-1**-mediated repression of **TGF-β** signaling, suggesting that HDAc is involved in transcriptional repression by **Evi-1**. This identifies a novel function of **Evi-1** as a member of corepressor complexes and suggests that aberrant recruitment of corepressors is one of the mechanisms involved in **Evi-1**-induced leukemogenesis. These results indicate that specific HDAc inhibitors may be useful in the treatment of **Evi-1**-induced neoplastic tumors, including myeloid leukemias.

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 10 OF 12 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:660563 HCAPLUS
DOCUMENT NUMBER: 135:317260
TITLE: TGIF2 interacts with histone deacetylase 1 and represses transcription
AUTHOR(S): Melhuish, Tiffany A.; Gallo, Christopher M.; Wotton, David
CORPORATE SOURCE: Department of Biochemistry and Molecular Genetics, University of Virginia, Charlottesville, VA, 22908, USA
SOURCE: Journal of Biological Chemistry (2001), 276(34), 32109-32114
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **TG-interacting factor** (**TGIF**) is a transcriptional repressor, which represses transcription by

binding directly to DNA or interacts with **transforming growth factor β (TGF.beta.)**-activated **Smads**, thereby repressing **TGFβ** -responsive gene expression. Mutation of **TGIF** in humans causes holoprosencephaly, a severe genetic disorder affecting craniofacial development. Searching human expressed sequence tag data bases revealed the presence of clones encoding a **TGIF**-related protein (TGIF2), which contains two regions of high sequence identity with **TGIF**. Here we show that, like **TGIF**, TGIF2 recruits histone deacetylase, but in contrast to **TGIF**, is unable to interact with the corepressor **CtBP**. TGIF2 and **TGIF** have very similar DNA-binding homeodomains, and TGIF2 represses transcription when bound to DNA via a **TGIF** binding site. TGIF2 interacts with **TGFβ** -activated **Smads** and represses **TGFβ** -responsive transcription. TGIF2 appears to be a context-independent transcriptional repressor, which can perform similar functions to **TGIF** and may play a role in processes, which, when disrupted by mutations in **TGIF**, cause holoprosencephaly.

REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 11 OF 12 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:330203 HCAPLUS
DOCUMENT NUMBER: 135:90686
TITLE: The corepressor **CtBP** interacts with **Evi-1** to repress **transforming growth factor β** signaling
AUTHOR(S): Izutsu, Koji; Kurokawa, Mineo; Imai, Yoichi; Maki, Kazuhiro; Mitani, Kinuko; Hirai, Hisamaru
CORPORATE SOURCE: Department of Hematology and Oncology, Graduate School of Medicine, University of Tokyo, Tokyo, 113-8655, Japan
SOURCE: Blood (2001), 97(9), 2815-2822
CODEN: BLOOAW; ISSN: 0006-4971
PUBLISHER: American Society of Hematology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **Evi-1** is a zinc finger nuclear protein whose inappropriate expression leads to leukemic transformation of hematopoietic cells in mice and humans. This was previously shown to block the antiproliferative effect of **transforming growth factor β (TGF-.beta.)**. **Evi-1** represses **TGF-.beta.** signaling by direct interaction with Smad3 through its first zinc finger motif. Here, it is demonstrated that **Evi-1** represses **Smad**-induced transcription by recruiting **C-terminal binding** protein (**CtBP**) as a corepressor. **Evi-1** assocs. with **CtBP1** through one of the consensus binding motifs, and this association is required for efficient inhibition of **TGF-β** signaling. A specific inhibitor for histone deacetylase (HDAc) alleviates **Evi-1**-mediated repression of **TGF-β** signaling, suggesting that HDAc is involved in the transcriptional repression

by **Evi-1**. This identifies a novel function of **Evi-1** as a member of corepressor complexes and suggests that aberrant recruitment of corepressors is one of the mechanisms for **Evi-1**-induced leukemogenesis.

REFERENCE COUNT: 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 12 OF 12 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:910882 HCAPLUS
DOCUMENT NUMBER: 134:174511
TITLE: The interaction of the carboxyl terminus-binding protein with the **Smad** corepressor **TGIF** is disrupted by a holoprosencephaly mutation in **TGIF**
AUTHOR(S): Melhuish, Tiffany A.; Wotton, David
CORPORATE SOURCE: Dep. Biochem. and Mol. Genet., Univ. Virginia, Charlottesville, VA, 22908, USA
SOURCE: Journal of Biological Chemistry (2000), 275(50), 39762-39766
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The homeodomain protein **TGIF** represses transcription in part by recruiting histone deacetylases. **TGIF** binds directly to DNA to repress transcription or interacts with **TGF**-β -activated **Smads**, thereby repressing genes normally activated by **TGF**-**.beta** .. Loss of function mutations in **TGIF** result in holoprosencephaly (HPE) in humans. One HPE mutation in **TGIF** results in a single amino acid substitution in a conserved PLDLS motif within the amino-terminal repression domain. It is demonstrated that **TGIF** interacts with the corepressor carboxyl terminus-binding protein (**CtBP**) via this motif. **CtBP**, which was first identified by its ability to bind the adenovirus E1A protein, interacts both with gene-specific transcriptional repressors and with a subset of polycomb proteins. Efficient repression of **TGF**-β -activated gene responses by **TGIF** is dependent on interaction with **CtBP**, and **TGIF** is able to recruit **CtBP** to a **TGF**-β -activated **Smad** complex. Disruption of the PLDLS motif in **TGIF** abolishes the interaction of **CtBP** with **TGIF** and compromises the ability of **TGIF** to repress transcription. Thus, at least one HPE mutation in **TGIF** appears to prevent **CtBP**-dependent transcriptional repression by **TGIF**, suggesting an important developmental role for the recruitment of **CtBP** by **TGIF**.

REFERENCE COUNT: 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 5 SEA FILE=REGISTRY ABB=ON PLU=ON "TRANSFORMING GROWTH FACTOR-B"?/CN
L5 41 SEA FILE=REGISTRY ABB=ON PLU=ON "TRANSFORMING GROWTH

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                FACTOR-B"?/CN
L6           46 SEA FILE=REGISTRY ABB=ON  PLU=ON  L4 OR L5
L7          184 SEA FILE=REGISTRY ABB=ON  PLU=ON  BONE MORPHOGENETIC
                PROTEIN ?/CN
L8          132 SEA FILE=REGISTRY ABB=ON  PLU=ON  ACTIVIN ?/CN
L9          361 SEA FILE=REGISTRY ABB=ON  PLU=ON  L6 OR L7 OR L8
L10       31551 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L9 OR (TRANSFORM?
                GROWTH FACTOR OR TGF)(W)(B OR BETA) OR ACTIVIN OR BONE
                MORPHOGENET? PROTEIN OR BMP OR TGFB
L11        1640 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L10 AND (SMAD OR EVI1
                OR EVII OR (EVI OR SIP)(W)(1 OR I) OR TGIF OR SIP1 OR
                SIPI OR SCHNURRI OR DROSOPHIL?(S)(MAD OR MEDEA MOTHER?(2W
                )DPP) OR TG(W)INTERACT?(W)FACTOR OR SHN)
L13          12 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L11 AND (CTBP# OR
                DCTBP# OR (C OR CARBOXY?)(W)TERMIN?(W)BIND?)


L14           0 L13 NOT L12

     (FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH,
     JICST-EPLUS, JAPIO' ENTERED AT 11:46:03 ON 31 OCT 2003)
L15          26 S L13
L16          13 DUP REM L15 (13 DUPLICATES REMOVED)

L16  ANSWER 1 OF 13  SCISEARCH  COPYRIGHT 2003 THOMSON ISI on STN
ACCESSION NUMBER:    2003:721093  SCISEARCH
THE GENUINE ARTICLE: 712BR
TITLE:               Transforming growth
                     factor beta 1 receptor II is
                     downregulated by E1A in adenovirus-infected cells
AUTHOR:              Tarakanova V L (Reprint); Wold W S M
CORPORATE SOURCE:    St Louis Univ, Sch Med, Dept Mol Microbiol &
                     Immunol, 1402 S Grand Blvd, St Louis, MO 63104 USA
                     (Reprint); St Louis Univ, Sch Med, Dept Mol
                     Microbiol & Immunol, St Louis, MO 63104 USA
COUNTRY OF AUTHOR:   USA
SOURCE:              JOURNAL OF VIROLOGY, (SEP 2003) Vol. 77, No. 17, pp.
                     9324-9336.
                     Publisher: AMER SOC MICROBIOLOGY, 1752 N ST NW,
                     WASHINGTON, DC 20036-2904 USA.
                     ISSN: 0022-538X.
DOCUMENT TYPE:       Article; Journal
LANGUAGE:            English
REFERENCE COUNT:     62
                    *ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*
AB       Transforming growth factor beta1 (TGF-beta1) signaling is
     compromised in many tumors, thereby allowing the tumor to escape the
     growth-inhibitory and proapoptotic activities of the cytokine. Human
     adenoviruses interfere with a number of cellular pathways involved
     in cell cycle regulation and apoptosis, initially placing the cell
     in a "tumor-like" state by forcing quiescent cells into the cell
     cycle and also inhibiting apoptosis. We report that
     adenovirus-infected cells resemble tumor cells in that TGF-beta1
     signaling is inhibited. The levels of TGF-beta1 receptor II
     (TbetaRII) in adenovirus-infected cells were decreased, and this
     decrease was mapped, by using virus mutants, to the E1A gene and to
     amino acids 2 to 36 and the C-terminal
     binding protein binding site in the E1A protein. The
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decrease in the TbetaRII protein was accompanied by a decrease in TbetaRII mRNA. The decrease in TbetaRII protein levels in adenovirus-infected cells was greater than the decrease in TbetaRII mRNA, suggesting that downregulation of the TbetaRII protein may occur through more than one mechanism. Surprisingly in this context, the half-lives of the TbetaRII protein in infected and uninfected cells were similar. TGF-beta1 signaling was compromised in cells infected with wild-type adenovirus, as measured with 3TP-lux, a **TGF-beta**-sensitive reporter plasmid expressing luciferase. Adenovirus mutants deficient in TbetaRII downregulation did not inhibit TGF-beta1 signaling. TGF-beta1 pretreatment reduced the relative abundance of adenovirus structural proteins in infected cells, an effect that was potentiated when cells were infected with mutants incapable of modulating the **TGF-beta** signaling pathway. These results raise the possibility that inhibition of **TGF-beta** signaling by E1A is a means by which adenovirus counters the antiviral defenses of the host.

L16 ANSWER 2 OF 13 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2003221346 MEDLINE
DOCUMENT NUMBER: 22627838 PubMed ID: 12743039
TITLE: Regulation of **Smad** signaling through a differential recruitment of coactivators and corepressors by ZEB proteins.
AUTHOR: Postigo Antonio A; Depp Jennifer L; Taylor Jennifer J; Kroll Kristen L
CORPORATE SOURCE: Division of Molecular Oncology, Department of Internal Medicine, Washington University School of Medicine, St Louis, MO 63110, USA..
apostigo@im.wustl.edu
SOURCE: EMBO JOURNAL, (2003 May 15) 22 (10) 2453-62.
Journal code: 8208664. ISSN: 0261-4189.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200307
ENTRY DATE: Entered STN: 20030514
Last Updated on STN: 20030715
Entered Medline: 20030714

AB Balancing signals derived from the TGFbeta family is crucial for regulating cell proliferation and differentiation, and in establishing the embryonic axis during development. TGFbeta/**BMP** signaling leads to the activation and nuclear translocation of **Smad** proteins, which activate transcription of specific target genes by recruiting P/CAF and p300. The two members of the ZEB family of zinc finger factors (ZEB-1/deltaEF1 and ZEB-2/**SIP1**) regulate TGFbeta/**BMP** signaling in opposite ways: ZEB-1/deltaEF1 synergizes with **Smad**-mediated transcriptional activation, while ZEB-2/**SIP1** represses it. Here we report that these antagonistic effects by the ZEB proteins arise from the differential recruitment of transcriptional coactivators (p300 and P/CAF) and corepressors (**CtBP**) to the **Smads**. Thus, while ZEB-1/deltaEF1 binds to p300 and promotes the formation of a p300-**Smad** transcriptional complex, ZEB-2/**SIP1** acts as a repressor by recruiting **CtBP**. This model of regulation by

ZEB proteins also functions in vivo, where they have opposing effects on the regulation of TGFbeta family-dependent genes during Xenopus development.

L16 ANSWER 3 OF 13 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
ACCESSION NUMBER: 2003:445536 SCISEARCH
THE GENUINE ARTICLE: 680BU
TITLE: Opposing functions of ZEB proteins in the regulation of the **TGF beta/BMP** signaling pathway
AUTHOR: Postigo A A (Reprint)
CORPORATE SOURCE: Washington Univ, Sch Med, Dept Internal Med, Div Mol Oncol, St Louis, MO 63110 USA (Reprint)
COUNTRY OF AUTHOR: USA
SOURCE: EMBO JOURNAL, (15 MAY 2003) Vol. 22, No. 10, pp. 2443-2452.
Publisher: OXFORD UNIV PRESS, GREAT CLARENDON ST, OXFORD OX2 6DP, ENGLAND.
ISSN: 0261-4189.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 66

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Binding of TGFbeta/**BMP** factors to their receptors leads to translocation of **Smad** proteins to the nucleus where they activate transcription of target genes. The two-handed zinc finger proteins encoded by Zfhx1a and Zfhx1b, ZEB-1/deltaEF1 and ZEB-2/**SIP1**, respectively, regulate gene expression and differentiation programs in a number of tissues. Here I demonstrate that ZEB proteins are also crucial regulators of TGFbeta/**BMP** signaling with opposing effects on this pathway. Both ZEB proteins bind to **Smads**, but while ZEB-1/deltaEF1 synergizes with **Smad** proteins to activate transcription, promote osteoblastic differentiation and induce cell growth arrest, the highly related ZEB-2/**SIP1** protein has the opposite effect. Finally, the ability of TGFbeta to mediate transcription of TGFbeta-dependent genes and induce growth arrest depends on the presence of endogenous ZEB-1/deltaEF1 protein.

L16 ANSWER 4 OF 13 WPIDS COPYRIGHT 2003 THOMSON DERWENT on STN
ACCESSION NUMBER: 2003-657220 [62] WPIDS
DOC. NO. NON-CPI: N2003-523633
DOC. NO. CPI: C2003-179420
TITLE: Identifying compounds that interact with **Smad** protein (co-repressor), useful for treating diseases involving negative regulation of **transforming growth factor-beta** e.g. cancer and autoimmune disease.
DERWENT CLASS: B04 C06 D16 S03
INVENTOR(S): LAUGHON, A S
PATENT ASSIGNEE(S): (LAUG-I) LAUGHON A S; (WISC) WISCONSIN ALUMNI RES FOUND
COUNTRY COUNT: 100
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG

US 2002137662 A1 20020926 (200362)* 7
WO 2002076466 A1 20021003 (200362) EN
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG UZ VN YU ZA ZM ZW

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 2002137662 A1		US 2001-810385	20010316
WO 2002076466 A1		WO 2002-US8133	20020315

PRIORITY APPLN. INFO: US 2001-810385 20010316
AN 2003-657220 [62] WPIDS
AB US2002137662 A UPAB: 20030928
NOVELTY - Identifying compounds that directly interact with a **Smad** protein or a **Smad** protein co-repressor to prevent protein-protein or protein-DNA interactions required for repression of transcription induced by transforming growth factor (**TGF**)**-beta, activin** or **bone morphogenetic protein** (**BMP**) signaling in cells, is new.

DETAILED DESCRIPTION - Identifying compounds that directly interact with a **Smad** protein or a **Smad** protein co-repressor to prevent protein-protein or protein-DNA interactions required for repression of transcription induced by transforming growth factor (**TGF**)**-beta, activin** or **bone morphogenetic protein** (**BMP**) signaling in cells comprising:

(a) determining a first level of transcription detected in cells in the presence of a **Smad** protein and a **CtBP** (undefined) protein before addition of a test compound;

(b) contacting the cells with the test compound; and

(c) determining a second level of transcription detected in cells in the presence of a **Smad** protein and a **CtBP** protein after addition of the test compound, where a decrease in the level of repression of transcription induced by the presence of the **Smad** protein and the **CtBP** protein is indicative of the ability of the test compound to interfere with transcriptional repression and to prevent repression of transcription that is produced by a **TGF-beta, activin,** or **BMP** signal in cells.

INDEPENDENT CLAIMS are also included for the following:

(1) a composition identified by the method; and

(2) identifying a candidate gene that is directly and negatively regulated by **TGF-beta** signaling pathways through a **CtBP** protein comprising:

(a) determining a first level of **TGF-beta**-regulated target gene expression in the presence of **CtBP**;

(b) determining a second level of **TGF-beta**-regulated target gene expression in the absence of the **CtBP** protein; and

(c) comparing the first level of expression with the second level of expression, where dependence of **TGF-beta** -regulated gene expression on the presence of the **CtBP** protein is indicative of the ability of the candidate gene to be directly and negatively regulated by **CtBP** working in conjunction with the **Smad** protein.

ACTIVITY - Cytostatic; Immunosuppressive.

MECHANISM OF ACTION - **CtBP** inhibitor; **Smad** inhibitor; Negative regulator of **TGF-beta**. No biological data given.

USE - The compounds or genes identified through such assays would be useful in the development of drugs and therapeutics for treatment of cancer, autoimmune diseases, and other hereditary diseases that involve negative regulation by **TGF-beta** pathways.

Dwg.0/8

L16 ANSWER 5 OF 13 EMBASE COPYRIGHT 2003 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2002167636 EMBASE

TITLE: The t(3;21) fusion product, AML1/**Evi-1** blocks AML1-induced transactivation by recruiting **CtBP**.

AUTHOR: Izutsu K.; Kurokawa M.; Imai Y.; Ichikawa M.; Asai T.; Maki K.; Mitani K.; Hirai H.

CORPORATE SOURCE: H. Hirai, Department of Hematology, Graduate School of Medicine, University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-8655, Japan. hhirai-tky@umin.ac.jp

SOURCE: Oncogene, (18 Apr 2002) 21/17 (2695-2703). Refs: 58 ISSN: 0950-9232 CODEN: ONCNES

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 016 Cancer
022 Human Genetics
025 Hematology

LANGUAGE: English

SUMMARY LANGUAGE: English

AB AML1/**Evi-1** is a chimeric protein that is derived from t(3;21), found in blastic transformation of chronic myelogenous leukemia. It is composed of the N-terminal AML1 portion with the DNA-binding Runt domain and the C-terminal **Evi-1** portion. It has been shown to dominantly repress AML1-induced transactivation. The mechanism for it has been mainly attributed to competition with AML1 for the DNA-binding and for the interaction with PEBP2β (CBFβ), a partner protein which heterodimerizes with AML1. It was recently found that **Evi-1** interacts with **C-terminal binding** protein (**CtBP**) to repress **TGF-beta**.-induced transactivation. Here, we demonstrate that AML1/**Evi-1** interacts with **CtBP** in SKH1 cells, a leukemic cell line which endogenously overexpresses AML1/**Evi-1** and that AML1/**Evi-1** requires the interaction with **CtBP** to repress AML1-induced transactivation. The association with **CtBP** is also required when AML1/**Evi-1** blocks myeloid differentiation of 32Dcl3 cells induced by granulocyte

colony-stimulating factor. Taken together, it is suggested that one of the mechanisms for AML1/**Evi-1**-associated leukemogenesis should be an aberrant recruitment of a corepressor complex by the chimeric protein.

L16 ANSWER 6 OF 13 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2001466782 MEDLINE
DOCUMENT NUMBER: 21402964 PubMed ID: 11427533
TITLE: TGIF2 interacts with histone deacetylase 1 and represses transcription.
AUTHOR: Melhuish T A; Gallo C M; Wotton D
CORPORATE SOURCE: Department of Biochemistry and Molecular Genetics, University of Virginia, Charlottesville, Virginia 22908, USA.
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (2001 Aug 24) 276 (34) 32109-14.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200109
ENTRY DATE: Entered STN: 20010821
Last Updated on STN: 20030105
Entered Medline: 20010920

AB **TG-interacting factor** (**TGIF**) is a transcriptional repressor, which represses transcription by binding directly to DNA or interacts with **transforming growth factor beta** (**TGF beta**)-activated **Smads**, thereby repressing **TGF beta**-responsive gene expression. Mutation of **TGIF** in humans causes holoprosencephaly, a severe genetic disorder affecting craniofacial development. Searching human expressed sequence tag data bases revealed the presence of clones encoding a **TGIF**-related protein (TGIF2), which contains two regions of high sequence identity with **TGIF**. Here we show that, like **TGIF**, TGIF2 recruits histone deacetylase, but in contrast to **TGIF**, is unable to interact with the corepressor **CtBP**. TGIF2 and **TGIF** have very similar DNA-binding homeodomains, and TGIF2 represses transcription when bound to DNA via a **TGIF** binding site. TGIF2 interacts with **TGF beta**-activated **Smads** and represses **TGF beta**-responsive transcription. TGIF2 appears to be a context-independent transcriptional repressor, which can perform similar functions to **TGIF** and may play a role in processes, which, when disrupted by mutations in **TGIF**, cause holoprosencephaly.

L16 ANSWER 7 OF 13 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 2001340867 MEDLINE
DOCUMENT NUMBER: 21213556 PubMed ID: 11313276
TITLE: The corepressor **CtBP** interacts with **Evi-1** to repress **transforming growth factor beta** signaling.
AUTHOR: Izutsu K; Kurokawa M; Imai Y; Maki K; Mitani K; Hirai H
CORPORATE SOURCE: Department of Hematology and Oncology, Graduate

School of Medicine, University of Tokyo, Japan.
SOURCE: BLOOD, (2001 May 1) 97 (9) 2815-22.
Journal code: 7603509. ISSN: 0006-4971.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200106
ENTRY DATE: Entered STN: 20010618
Last Updated on STN: 20010618
Entered Medline: 20010614

AB **Evi-1** is a zinc finger nuclear protein whose inappropriate expression leads to leukemic transformation of hematopoietic cells in mice and humans. This was previously shown to block the antiproliferative effect of **transforming growth factor beta** (**TGF-beta**). **Evi-1** represses **TGF-beta** signaling by direct interaction with Smad3 through its first zinc finger motif. Here, it is demonstrated that **Evi-1** represses **Smad**-induced transcription by recruiting **C-terminal binding** protein (**CtBP**) as a corepressor. **Evi-1** associates with **CtBP1** through one of the consensus binding motifs, and this association is required for efficient inhibition of **TGF-beta** signaling. A specific inhibitor for histone deacetylase (HDAc) alleviates **Evi-1**-mediated repression of **TGF-beta** signaling, suggesting that HDAc is involved in the transcriptional repression by **Evi-1**. This identifies a novel function of **Evi-1** as a member of corepressor complexes and suggests that aberrant recruitment of corepressors is one of the mechanisms for **Evi-1**-induced leukemogenesis.

L16 ANSWER 8 OF 13 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2002:158361 BIOSIS
DOCUMENT NUMBER: PREV200200158361
TITLE: Recruitment of **TGIF** to polycomb group complexes.
AUTHOR(S): Melhuish, Tiffany A.; Wotton, David
SOURCE: Molecular Biology of the Cell, (Nov, 2001) Vol. 12, No. Supplement, pp. 490a. print.
Meeting Info.: 41st Annual Meeting of the American Society for Cell Biology. Washington DC, USA. December 08-12, 2001. American Society for Cell Biology.
CODEN: MBCEEV. ISSN: 1059-1524.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 21 Feb 2002
Last Updated on STN: 26 Feb 2002

L16 ANSWER 9 OF 13 JICST-EPlus COPYRIGHT 2003 JST on STN
ACCESSION NUMBER: 1020895481 JICST-EPlus
TITLE: Analysis of control mechanism of the **TGF**. **BETA**. signal in **Evi-1** (Ministry of Health,Labour and Welfare S).

AUTHOR: HIRAI HISAMARU; IZUTSU KOJI; KUROKAWA MINEO
CORPORATE SOURCE: Todai I Ketsuekishuyonaika
SOURCE: Tokuhatsusei Zoketsu Shogai ni kansuru Kenkyuhan. Heisei 12 Nendo Kenkyu Gyoseki Hokokusho, (2001) pp. 91-92. Journal Code: N20022248 (Fig. 4, Ref. 3)
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Short Communication
LANGUAGE: Japanese
STATUS: New

AB The deletion mutant of **Evi-1** was made, and this gene introduction was done with the p3TP-Lux reporter in the HepG32 cell, and the transcriptive activity by **TGF.BETA** . was examined. **Evi-1** It was clarified that the colearesor complex of the transfer which consists of **CtBP** -HDAc functioned, when it suppressed the **TGF.BETA** . signal by Smad3 combining. The treatment based on the new idea is expected this knowledge in myelodysplastic syndrome and myelocytic leukemia in which **Evi-1** is concerned in the crisis.

L16 ANSWER 10 OF 13 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 2001540678 MEDLINE
DOCUMENT NUMBER: 21470996 PubMed ID: 11587364
TITLE: Oncogenic mechanisms of **Evi-1** protein.
AUTHOR: Hirai H; Izutsu K; Kurokawa M; Mitani K
CORPORATE SOURCE: Department of Hematology and Oncology, Graduate School of Medicine, University of Tokyo, Hongo, Japan.. hhirai-tky@umin.ac.jp
SOURCE: CANCER CHEMOTHERAPY AND PHARMACOLOGY, (2001 Aug) 48 Suppl 1 S35-40. Ref: 29
Journal code: 7806519. ISSN: 0344-5704.
PUB. COUNTRY: Germany: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200110
ENTRY DATE: Entered STN: 20011008
Last Updated on STN: 20011015
Entered Medline: 20011011

AB Although **Evi-1** is thought to promote growth or block differentiation in some cell types, its biological functions have not been elucidated. To explore the mechanisms underlying **Evi-1**-induced oncogenesis, we investigated whether **Evi-1** affects the signaling of **transforming growth factor beta** (**TGF-beta**), which inhibits proliferation of a wide range of cell types and is one of the most studied growth regulatory factors. We demonstrated that **Evi-1** represses **TGF-beta** signaling and antagonizes its growth-inhibitory effects. Two separate regions of **Evi-1** are responsible for this repression, one of which is the first zinc-finger domain. Through this domain, **Evi-1** physically interacts with Smad3, an intracellular mediator of **TGF-beta** signaling, thereby suppressing the transcriptional activity of Smad3. These results define a novel

function of **Evi-1** as a repressor of signaling components of **TGF-beta**. We also demonstrated that **Evi-1** represses **Smad**-induced transcriptional activation by recruiting **CtBP** as a corepressor. **Evi-1** associates with **CtBP1** through one of the **CtBP**-binding consensus motifs within the region from amino acid 544 to 607, and this association is required for the efficient inhibition of **TGF -beta** signaling. A specific histone deacetylase (HDAc) inhibitor, trichostatin A (TSA), alleviates **Evi-1** -mediated repression of **TGF-beta** signaling, suggesting that HDAc is involved in transcriptional repression by **Evi-1**. This identifies a novel function of **Evi-1** as a member of corepressor complexes and suggests that aberrant recruitment of corepressors is one of the mechanisms involved in **Evi-1**-induced leukemogenesis. These results indicate that specific HDAc inhibitors may be useful in the treatment of **Evi-1** -induced neoplastic tumors, including myeloid leukemias.

L16 ANSWER 11 OF 13 MEDLINE on STN DUPLICATE 5
ACCESSION NUMBER: 2001106053 MEDLINE
DOCUMENT NUMBER: 20564354 PubMed ID: 10995736
TITLE: The interaction of the **carboxyl terminus-binding** protein with the **Smad** corepressor **TGIF** is disrupted by a holoprosencephaly mutation in **TGIF**.
AUTHOR: Melhuish T A; Wotton D
CORPORATE SOURCE: Department of Biochemistry and Molecular Genetics and Center for Cell Signaling, University of Virginia, Charlottesville, Virginia 22908, USA.
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (2000 Dec 15) 275 (50) 39762-6.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200102
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20010208

AB The homeodomain protein **TGIF** represses transcription in part by recruiting histone deacetylases. **TGIF** binds directly to DNA to repress transcription or interacts with **TGF-beta**-activated **Smads**, thereby repressing genes normally activated by **TGF-beta**. Loss of function mutations in **TGIF** result in holoprosencephaly (HPE) in humans. One HPE mutation in **TGIF** results in a single amino acid substitution in a conserved PLDLS motif within the amino-terminal repression domain. We demonstrate that **TGIF** interacts with the corepressor **carboxyl terminus-binding** protein (**CtBP**) via this motif. **CtBP**, which was first identified by its ability to bind the adenovirus E1A protein, interacts both with gene-specific transcriptional repressors and with a subset of polycomb proteins. Efficient repression of **TGF-beta**-activated gene responses by **TGIF** is dependent on interaction with

CtBP, and we show that **TGIF** is able to recruit **CtBP** to a **TGF-beta**-activated **Smad** complex. Disruption of the PLDLS motif in **TGIF** abolishes the interaction of **CtBP** with **TGIF** and compromises the ability of **TGIF** to repress transcription. Thus, at least one HPE mutation in **TGIF** appears to prevent **CtBP**-dependent transcriptional repression by **TGIF**, suggesting an important developmental role for the recruitment of **CtBP** by **TGIF**.

L16 ANSWER 12 OF 13 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN

ACCESSION NUMBER: 2001:301470 BIOSIS
DOCUMENT NUMBER: PREV200100301470
TITLE: The corepressor **CTBP** is involved in **Evi-1** mediated repression of **TGF-beta** signaling.
AUTHOR(S): Izutsu, Koji [Reprint author]; Kurokawa, Mineo [Reprint author]; Imai, Yoichi [Reprint author]; Mitani, Kinuko [Reprint author]; Hirai, Hisamaru [Reprint author]
CORPORATE SOURCE: Department of Hematology and Oncology, Graduate School of Medicine, University of Tokyo, Tokyo, Japan
SOURCE: Blood, (November 16, 2000) Vol. 96, No. 11 Part 1, pp. 90a. print.
Meeting Info.: 42nd Annual Meeting of the American Society of Hematology. San Francisco, California, USA. December 01-05, 2000. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 27 Jun 2001
Last Updated on STN: 19 Feb 2002

AB **Evi-1** is a zinc finger nuclear protein whose inappropriate expression leads to leukemic transformation of hematopoietic cells in mice and humans. **Evi-1** is shown to be highly expressed in human myeloid leukemias and myelodysplastic syndromes by chromosomal rearrangements involving 3q26. It is also aberrantly expressed as a fusion transcript with AML1 (AML1/**Evi-1**), which leads to blastic transformation in patients with chronic myelogenous leukemia. We previously showed that **Evi-1** and AML1/**Evi-1** block the antiproliferative effect of **TGF-beta**. They represses **TGF-beta** signaling by direct interaction with Smad3 through their first zinc finger motif. Here, we demonstrate that **Evi-1** represses **Smad**-induced transcription by recruiting **CtBP** as a corepressor. **CtBP** was originally identified as a protein which interacts with C-terminal region of adenoviral oncoprotein E1A. **CtBP** is ubiquitously expressed including hematopoietic cells, and has been shown to act as a corepressor of certain transcriptional repressors, such as BKLF, FOG, and TCF. We show that **Evi-1** directly associates with **CtBP1** through one of the consensus binding motifs, and this association is required for efficient inhibition of **TGF-beta** signaling. A

specific inhibitor for histone deacetylase (HDAc) alleviates **Evi-1**-mediated repression of **TGF-beta** signaling, suggesting that HDAc is involved in the transcriptional repression by **Evi-1**. This identifies a novel function of **Evi-1** as a member of corepressor complexes and suggests that aberrant recruitment of corepressors is one of the mechanisms for **Evi-1**-induced leukemogenesis.

L16 ANSWER 13 OF 13 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
ACCESSION NUMBER: 2001:74793 SCISEARCH
THE GENUINE ARTICLE: 372WB
TITLE: The corepressor **CtBP** is involved in **Evi-1** mediated repression of **TGF-beta** signaling.
AUTHOR: Izutsu K (Reprint); Kurokawa M; Imai Y; Mitani K; Hirai H
CORPORATE SOURCE: Univ Tokyo, Grad Sch Med, Dept Hematol & Oncol, Tokyo, Japan
COUNTRY OF AUTHOR: Japan
SOURCE: BLOOD, (16 NOV 2000) Vol. 96, No. 11, Part 1, pp. 90A-90A. MA 385.
Publisher: AMER SOC HEMATOLOGY, 1900 M STREET. NW SUITE 200, WASHINGTON, DC 20036 USA.
ISSN: 0006-4971.
DOCUMENT TYPE: Conference; Journal
LANGUAGE: English
REFERENCE COUNT: 0

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